

U.S. Patent Application No. 10/058,069  
Attorney Ref. No.: 037003-0280727

## I. AMENDMENT

### Amendment of the claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-19. (Canceled)

20. (Currently amended) A kit useful for the treatment of a mammal suffering from or predisposed to a neoplastic disorder comprising at least one container having a dimeric antibody that binds specifically to TAG-72 deposited therein;

which dimeric antibody comprises two antibodies that are non-covalently associated to form a tetravalent antibody dimer having four antigen-binding sites that bind specifically to TAG-72,

wherein each of the antibodies in the dimer comprises two antibody heavy chain polypeptides having the heavy chain variable region amino acid sequence shown in Figure 4A (SEQ ID NO: 7), and two antibody light chain polypeptides having the light chain variable region amino acid sequence shown in Figure 5A (SEQ ID NO: 9), and has two antigen-binding sites that bind specifically to TAG-72; and

wherein a  $C_H2$  domain is deleted from, and a  $C_H3$  domain is fused directly to the hinge region of each of the four antibody heavy chain polypeptides in the dimeric antibody;

and further comprising a label or an insert indicating that said dimeric antibody may be used to treat said neoplastic disorder.

21-28. (Canceled)

29. (Currently amended) A dimeric antibody that binds specifically to TAG-72, which dimeric antibody comprises two antibodies that are non-covalently associated to form a tetravalent antibody dimer having four antigen-binding sites that bind specifically to TAG-72,

wherein each of the antibodies in the dimer comprises two antibody heavy chain polypeptides having the heavy chain variable region amino acid sequence shown in Figure 4A (SEQ ID NO: 7), and two antibody light chain polypeptides having the light chain variable region amino acid sequence shown in Figure 5A (SEQ ID NO: 9), and has two antigen-binding sites that bind specifically to TAG-72; and

wherein a  $C_H2$  domain is deleted from, and a  $C_H3$  domain is fused directly to the hinge region of each of the four antibody heavy chain polypeptides in the dimeric antibody.

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30-37. (Canceled)

38. (Previously presented) The dimeric antibody of claim 29 wherein said dimeric antibody is conjugated to a cytotoxic agent.

39. (Original) The dimeric antibody of claim 38 wherein said cytotoxic agent comprises a radioisotope.

40. (Original) The dimeric antibody of claim 39 wherein said radioisotope is selected from the group consisting of  $^{90}\text{Y}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{123}\text{I}$ ,  $^{111}\text{In}$ ,  $^{105}\text{Rh}$ ,  $^{153}\text{Sm}$ ,  $^{67}\text{Cu}$ ,  $^{67}\text{Ga}$ ,  $^{166}\text{Ho}$ ,  $^{177}\text{Lu}$ ,  $^{186}\text{Re}$  and  $^{188}\text{Re}$ .

41-54. (Canceled)

55. (Currently amended) The kit of claim 20, wherein said antibody dimer ~~is a chimeric antibody comprising~~ comprises human antibody constant regions.

56-61. (Canceled)

62. (Previously presented) The kit of claim 55, wherein said antibody dimer comprises four antibody heavy chain polypeptides having the heavy chain polypeptide amino acid sequence shown in Figure 4A (SEQ ID NO: 7), and four antibody light chain polypeptides having the light chain polypeptide amino acid sequence shown in Figure 5A (SEQ ID NO: 9).

63. (Previously presented) The kit of claim 20 wherein said neoplastic disorder is colon cancer.

64-67. (Canceled)

68. (Currently amended) The dimeric antibody of claim 29, wherein said antibody dimer ~~is a chimeric antibody comprising~~ comprises human antibody constant regions.

69-74. (Canceled)

75. (Previously presented) The dimeric antibody of claim 68, wherein said antibody dimer comprises four antibody heavy chain polypeptides having the heavy chain polypeptide amino acid sequence shown in Figure 4A (SEQ ID NO: 7), and four antibody light chain polypeptides having the light chain polypeptide amino acid sequence shown in Figure 5A (SEQ ID NO: 9).

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76. (Previously presented) The dimeric antibody of claim 38, wherein said cytotoxic agent is selected from the group consisting of cytostatic agents, alkylating agents, antimetabolites, anti-proliferative agents, tubulin binding agents, hormones and hormone antagonists, anthracycline drugs, vinca drugs, mitomycins, bleomycins, cytotoxic nucleosides, pteridine drugs, diynes, podophyllotoxins, toxic enzymes, and radiosensitizing drugs.

77. (Previously presented) The dimeric antibody of claim 76, wherein said cytotoxic agent is selected from the group consisting of mechlorethamine, triethylenephosphoramide, cyclophosphamide, ifosfamide, chlorambucil, busulfan, melphalan, triaziquone, nitrosourea compounds, adriamycin, carminomycin, daunorubicin (daunomycin), doxorubicin, aminopterin, methotrexate, methopterin, mithramycin, streptonigrin, dichloromethotrexate, mitomycin C, actinomycin-D, porfiromycin, 5-fluorouracil, floxuridine, ftorafur, 6-mercaptopurine, cytarabine, cytosine arabinoside, podophyllotoxin, etoposide, etoposide phosphate, melphalan, vinblastine, vincristine, leurosine, vindesine, leurosine, taxol, taxane, cytochalasin B, gramicidin D, ethidium bromide, emetine, tenoposide, colchicin, dihydroxy anthracin dione, mitoxantrone, procaine, tetracaine, lidocaine, propranolol, puromycin, ricin subunit A, abrin, diphtheria toxin, botulinum, cyanginosins, saxitoxin, shigatoxin, tetanus, tetrodotoxin, trichothecene, verrucologen, corticosteroids, progestins, estrogens, antiestrogens, androgens, aromatase inhibitors, calicheamicin, esperamicins, and dynemicins.

78. (Previously presented) The dimeric antibody of claim 76, wherein said hormone or hormone antagonist is selected from the group consisting of prednisone, hydroxyprogesterone, medroprogesterone, diethylstilbestrol, tamoxifen, testosterone, and aminogluthetamide.

79. (Previously presented) The dimeric antibody of claim 38, wherein said cytotoxic agent is a prodrug selected from the group consisting of phosphate-containing prodrugs, thiophosphate-containing prodrugs, sulfate containing prodrugs, peptide containing prodrugs,  $\beta$ -lactam-containing prodrugs, optionally substituted phenoxyacetamide-containing prodrugs, optionally substituted phenylacetamide-containing prodrugs, 5-fluorocytosine, and 5-fluorouridine prodrugs that can be converted to the more active cytotoxic free drug.

80. (Currently amended) A kit useful for the treatment of a mammal suffering from or predisposed to a neoplastic disorder comprising at least one container having a dimeric antibody that binds specifically to TAG-72 deposited therein,;

which dimeric antibody comprises two antibodies that are non-covalently associated to form a tetravalent antibody dimer having four antigen-binding sites that bind specifically to TAG-72,

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wherein each of the antibodies in the dimer comprises two antibody heavy chain polypeptides having the heavy chain polypeptide amino acid sequence shown in Figure 4A (SEQ ID NO: 7), and two antibody light chain polypeptides having the light chain polypeptide amino acid sequence shown in Figure 5A (SEQ ID NO: 9), and has two antigen-binding sites that bind specifically to TAG-72; and

wherein a C<sub>H</sub>2 domain is deleted from, and a C<sub>H</sub>3 domain is fused directly to the hinge region of each of the four antibody heavy chain polypeptides in the dimeric antibody;

and further comprising a label or an insert indicating that said dimeric antibody may be used to treat said neoplastic disorder.

81. (Currently amended) The kit of claim 80, wherein said antibody dimer is ~~a chimeric antibody comprising~~ comprises human antibody constant regions.

82-83. (Canceled)

84. (Previously presented) The kit of claim 80 wherein said neoplastic disorder is colon cancer.

85. (Currently amended) A dimeric antibody that binds specifically to TAG-72, which dimeric antibody comprises two antibodies that are non-covalently associated to form a tetravalent antibody dimer having four antigen-binding sites that bind specifically to TAG-72.

wherein each of the antibodies in the dimer comprises two antibody heavy chain polypeptides having the heavy chain polypeptide amino acid sequence shown in Figure 4A (SEQ ID NO: 7), and two antibody light chain polypeptides having the light chain polypeptide amino acid sequence shown in Figure 5A (SEQ ID NO: 9), and has two antigen-binding sites that bind specifically to TAG-72; and

wherein a C<sub>H</sub>2 domain is deleted from, and a C<sub>H</sub>3 domain is fused directly to the hinge region of each of the four antibody heavy chain polypeptides in the dimeric antibody.

86. (Previously presented) The dimeric antibody of claim 85 wherein said dimeric antibody is conjugated to a cytotoxic agent.

87. (Previously presented) The dimeric antibody of claim 85 wherein said cytotoxic agent comprises a radioisotope.

88. (Previously presented) The dimeric antibody of claim 85 wherein said radioisotope is selected from the group consisting of <sup>90</sup>Y, <sup>125</sup>I, <sup>131</sup>I, <sup>123</sup>I, <sup>111</sup>In, <sup>105</sup>Rh, <sup>153</sup>Sm, <sup>67</sup>Cu, <sup>67</sup>Ga, <sup>166</sup>Ho, <sup>177</sup>Lu, <sup>186</sup>Re and <sup>188</sup>Re.

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89. (Previously presented) The dimeric antibody of claim 86, wherein said cytotoxic agent is selected from the group consisting of cytostatic agents, alkylating agents, antimetabolites, anti-proliferative agents, tubulin binding agents, hormones and hormone antagonists, anthracycline drugs, vinca drugs, mitomycins, bleomycins, cytotoxic nucleosides, pteridine drugs, diylenes, podophyllotoxins, toxic enzymes, and radiosensitizing drugs.

90. (Previously presented) The dimeric antibody of claim 89, wherein said cytotoxic agent is selected from the group consisting of mechlorethamine, triethylenephosphoramide, cyclophosphamide, ifosfamide, chlorambucil, busulfan, melphalan, triaziquone, nitrosourea compounds, adriamycin, carminomycin, daunorubicin (daunomycin), doxorubicin, aminopterin, methotrexate, methopterin, mithramycin, streptonigrin, dichloromethotrexate, mitomycin C, actinomycin-D, porfiromycin, 5-fluorouracil, floxuridine, ftorafur, 6-mercaptopurine, cytarabine, cytosine arabinoside, podophyllotoxin, etoposide, etoposide phosphate, melphalan, vinblastine, vincristine, leurosine, vindesine, leurosine, taxol, taxane, cytochalasin B, gramicidin D, ethidium bromide, emetine, tenoposide, colchicin, dihydroxy anthracin dione, mitoxantrone, procaine, tetracaine, lidocaine, propranolol, puromycin, ricin subunit A, abrin, diphtheria toxin, botulinum, cyanginosins, saxitoxin, shigatoxin, tetanus, tetrodotoxin, trichothecene, verrucologen, corticosteroids, progestins, estrogens, antiestrogens, androgens, aromatase inhibitors, calicheamicin, esperamicins, and dynemicins.

91. (Previously presented) The dimeric antibody of claim 89, wherein said hormone or hormone antagonist is selected from the group consisting of prednisone, hydroxyprogesterone, medroprogesterone, diethylstilbestrol, tamoxifen, testosterone, and aminogluthetamide.

92. (Previously presented) The dimeric antibody of claim 86, wherein said cytotoxic agent is a prodrug selected from the group consisting of phosphate-containing prodrugs, thiophosphate-containing prodrugs, sulfate containing prodrugs, peptide containing prodrugs,  $\beta$ -lactam-containing prodrugs, optionally substituted phenoxyacetamide-containing prodrugs, optionally substituted phenylacetamide-containing prodrugs, 5-fluorocytosinem, and 5-fluorouridine prodrugs that can be converted to the more active cytotoxic free drug.